

WHAT IS CLAIMED IS:

1. An isolated antibody or epitope-binding fragment thereof, comprising at least one complementarity-determining region having an amino acid sequence selected from the group consisting of SEQ ID NOs:1-6:

SYYYIH (SEQ ID NO:1),
VIYPGNDDISYNQKFXG (SEQ ID NO:2), wherein X is K or Q,
EVRLRYFDV (SEQ ID NO:3),
KSSQSVFFSSSQKNYLA (SEQ ID NO:4),
WASTRES (SEQ ID NO:5),
HQYLSSRT (SEQ ID NO:6),

and having the ability to bind CD33.

2. An antibody or epitope-binding fragment thereof, comprising at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarity-determining regions having amino acid sequences represented by SEQ ID NOs:1-3, respectively,

SYYYIH (SEQ ID NO:1),
VIYPGNDDISYNQKFXG (SEQ ID NO:2), wherein X is K or Q,
EVRLRYFDV (SEQ ID NO:3),

and wherein said light chain variable region comprises three complementarity-determining regions having amino acid sequences represented by SEQ ID NOs:4-6, respectively,

KSSQSVFFSSSQKNYLA (SEQ ID NO:4),
WASTRES (SEQ ID NO:5),
HQYLSSRT (SEQ ID NO:6).

3. The antibody or epitope-binding fragment thereof of claim 2, wherein said heavy chain variable region has at least 90% sequence identity to an amino acid sequence represented by SEQ ID NO:7:

QVQLQQPGAEEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFKGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGAGT
TVTVSS.

4. The antibody or epitope-binding fragment thereof of claim 2, wherein said heavy chain variable region has at least 95% sequence identity to said amino acid sequence represented by SEQ ID NO:7:

QVQLQQPGAEEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFKGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGAGT
TVTVSS.

5. The antibody or epitope-binding fragment thereof of claim 2, wherein said heavy chain variable region has an amino acid sequence represented by SEQ ID NO:7:

QVQLQQPGAEEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFKGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGAGT
TVTVSS.

6. The antibody or epitope-binding fragment thereof of claim 2, wherein said light chain variable region has at least 90% sequence identity to an amino acid sequence represented by SEQ ID NO:8:

NIMLTQSPSSLAVSAGEKVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPKLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVQSEDLAIYYCHQYLSSRTFGGGTKLEIKR.

7. The antibody or epitope-binding fragment thereof of claim 2, wherein said light chain variable region has at least 95% sequence identity to said amino acid sequence represented by SEQ ID NO:8:

NIMLTQSPSSLAVSAGEKVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPKLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVQSEDLAIYYCHQYLSSRTFGGGTKLEIKR.

8. The antibody or epitope-binding fragment thereof of claim 2, wherein said light chain variable region has an amino acid sequence that is represented by SEQ ID NO:8:
NIMLTQSPSSLAVSAGEKVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPKLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVQSEDLAIYYCHQYLSSRTFGGGTKLEIKR.

9. The antibody or epitope-binding fragment thereof of claim 2, wherein said heavy chain variable region has at least 90% sequence identity to an amino acid sequence represented by SEQ ID NO:9:
QVQLQQPGAEEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFQGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGQGT
TVTVSS.

10. The antibody or epitope-binding fragment thereof of claim 2, wherein said heavy chain variable region has at least 95% sequence identity to said amino acid sequence represented by SEQ ID NO:9:
QVQLQQPGAEEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFQGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGQGT
TVTVSS.

11. The antibody or epitope-binding fragment thereof of claim 2, wherein said heavy chain variable region has an amino acid sequence represented by SEQ ID NO:9:

QVQLQQPGAIEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFQGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGQGT
TVTVSS.

12. The antibody or epitope-binding fragment thereof of claim 2, wherein said light chain variable region has at least 90% sequence identity to an amino acid sequence represented by SEQ ID NO:10:

EIVLTQSPGSLAVSPGERVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPRLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVQPEDLAIYYCHQYLSSRTFGQGGTKLEIKR.

13. The antibody or epitope-binding fragment thereof of claim 2, wherein said light chain variable region has at least 95% sequence identity to said amino acid sequence represented by SEQ ID NO:10:

EIVLTQSPGSLAVSPGERVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPRLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVQPEDLAIYYCHQYLSSRTFGQGGTKLEIKR.

14. The antibody or epitope-binding fragment thereof of claim 2, wherein said light chain variable region has an amino acid sequence that is represented by SEQ ID NO:10:
EIVLTQSPGSLAVSPGERVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPRLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVQPEDLAIYYCHQYLSSRTFGQGGTKLEIKR.

15. A purified antibody or epitope-binding fragment thereof that specifically binds to CD33, wherein the heavy chain variable region portion of said antibody or epitope-binding fragment has an amino acid sequence represented by SEQ ID NO:7:

QVQLQQPGAIEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFQKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGAGT
TVTVSS, and wherein the light chain variable region portion of said antibody or epitope-binding fragment has an amino acid sequence represented by SEQ ID NO:8:

NIMLTQSPSSLAVSAGEKVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPKLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVVQSEDLAIYYCHQYLSSRTFGGGGTKLEIKR.

16. A humanized or resurfaced antibody, or an epitope-binding fragment thereof, that specifically binds to CD33, wherein the heavy chain variable region portion of said antibody or epitope-binding fragment has an amino acid sequence represented by SEQ ID NO:9:

QVQLQQPGAEEVVKPGASVKMSCKASGYTFTSYIHWIKQTPGQGLEWVGVIYPGND
DISYNQKFQGKATLTADKSSTTAYMQLSSLTSEDSAVYYCAREVRLRYFDVWGQGT
TVTVSS, and wherein the light chain variable region portion of said antibody or epitope-binding fragment has an amino acid sequence represented by SEQ ID NO:10:

EIVLTQSPGSLAVSPGERVTMSCKSSQSVFFSSSQKNYLAWYQQIPGQSPRLLIYWAS
TRESGVPDRFTGSGSGTDFTLTISVVQPEDLAIYYCHQYLSSRTFGQGGTKLEIKR.

17. An immunoconjugate comprising the antibody or epitope-binding fragment thereof of claim 1 linked to a drug or prodrug.

18. An immunoconjugate comprising the antibody or epitope-binding fragment thereof of claim 2 linked to a drug or prodrug.

19. The immunoconjugate of claim 17, wherein said drug or prodrug is selected from the group consisting of a maytansinoid, a taxoid, CC-1065, a CC-1065 analog, dolastatin, a dolastatin analog, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, melphalan, mitomycin C, chlorambucil, calicheamicin, and derivatives thereof.

20. The immunoconjugate of claim 18, wherein said drug or prodrug is selected from the group consisting of a maytansinoid, a taxoid, CC-1065, a CC-1065 analog, dolastatin, a dolastatin analog, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, melphalan, mitomycin C, chlorambucil, calicheamicin, and derivatives thereof.

21. A composition comprising the antibody or epitope-binding fragment thereof of claim 1 and a drug or prodrug.

22. A composition comprising the antibody or epitope-binding fragment thereof of claim 2 and a drug or prodrug.

23. A pharmaceutical composition comprising the antibody or epitope-binding fragment thereof of claim 1, and a pharmaceutically acceptable agent.

24. A pharmaceutical composition comprising the antibody or epitope-binding fragment thereof of claim 2, and a pharmaceutically acceptable agent.

25. A pharmaceutical composition comprising the immunoconjugate of claim 17, and a pharmaceutically acceptable agent.

26. A pharmaceutical composition comprising the immunoconjugate of claim 18, and a pharmaceutically acceptable agent.

27. A pharmaceutical composition comprising the composition of claim 21, and a pharmaceutically acceptable agent.

28. A pharmaceutical composition comprising the composition of claim 22, and a pharmaceutically acceptable agent.

29. A diagnostic reagent comprising the antibody of claim 1, wherein said antibody or antibody fragment is labeled.

30. A diagnostic reagent comprising the antibody of claim 2, wherein said antibody or antibody fragment is labeled.

31. The diagnostic reagent of claim 29, wherein said label is selected from the group consisting of a biotin label, an enzyme label, a radio-label, a fluorophore, a chromophore, an imaging agent and a metal ion.

32. The diagnostic reagent of claim 30, wherein said label is selected from the group consisting of a biotin label, an enzyme label, a radio-label, a fluorophore, a chromophore, an imaging agent and a metal ion.

33. A method for inhibiting the growth of a cell expressing CD33 comprising contacting said cell with the antibody or epitope-binding fragment thereof of claim 1 or 2.

34. A method for inhibiting the growth of a cell expressing CD33 comprising contacting said cell with the immunoconjugate of claim 17 or 18.

35. A method for inhibiting the growth of a cell expressing CD33 comprising contacting said cell with the composition of claim 21 or 22.

36. A method for inhibiting the growth of a cell expressing CD33 comprising contacting said cell with a pharmaceutical composition selected from claims 23-28.

37. A method for treating a subject having a disease wherein CD33 is expressed, comprising administering to said subject an effective amount of the antibody or epitope-binding fragment thereof of claim 1 or 2.

38. A method for treating a subject having a disease wherein CD33 is expressed, comprising administering to said subject an effective amount of the immunoconjugate of claim 17 or 18.

39. A method for treating a subject having a disease wherein CD33 is expressed, comprising administering to said subject an effective amount of the composition of claim 21 or 22.

40. A method for treating a subject having a disease wherein CD33 is expressed, comprising administering to said subject an effective amount of the pharmaceutical composition of claim 23 or 24.

41. A method for treating a subject having a disease wherein CD33 is expressed, comprising administering to said subject an effective amount of the pharmaceutical composition of claim 25 or 26.

42. A method for treating a subject having a disease wherein CD33 is expressed, comprising administering to said subject an effective amount of the pharmaceutical composition of claim 27 or 28.

43. A method for treating a subject having a disease wherein CD33 is expressed, comprising contacting one or more cells of said subject *ex vivo* with an effective amount of the antibody or epitope-binding fragment thereof of claim 1 or 2.

44. A method for treating a subject having a disease wherein CD33 is expressed, comprising contacting one or more cells of said subject *ex vivo* with an effective amount of an immunoconjugate of claim 17 or 18.

45. A method for treating a subject having a disease wherein CD33 is expressed, comprising contacting one or more cells of said subject *ex vivo* with an effective amount of a composition of claim 21 or 22.

46. A method for treating a subject having a disease wherein CD33 is expressed, comprising contacting one or more cells of said subject *ex vivo* with an effective amount of a pharmaceutical composition selected from claims 23-28.

47. The method of treatment of claim 37, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

48. The method of treatment of claim 38, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

49. The method of treatment of claim 39, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

50. The method of treatment of claim 40, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

51. The method of treatment of claim 41, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

52. The method of treatment of claim 42, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

53. The method of treatment of claim 43, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

54. The method of treatment of claim 44, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

55. The method of treatment of claim 45, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

56. The method of treatment of claim 46, wherein said disease is a disease selected from the group consisting of myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

57. A method of determining whether a biological sample contains a myelogenous cancer cell, comprising:

- (a) contacting said biological sample with a diagnostic reagent of claim 29 or 30, and
- (b) detecting the distribution of said reagent within said sample.

58. The method of diagnosis of claim 57, wherein said cancer is a cancer selected from the group consisting of acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and pro-myelocytic leukemia (PML).

59. An improved antibody or epitope-binding fragment thereof that specifically binds to CD33, said improved antibody or antibody fragment prepared by:

- (a) providing a DNA that encodes an antibody or epitope-binding fragment thereof comprising at least one of SEQ ID NO:7 and SEQ ID NO:8,
- (b) introducing at least one nucleotide mutation, deletion, insertion or addition into said DNA such that the amino acid sequence of said antibody or epitope-binding fragment encoded by said DNA is changed;
- (c) expressing said antibody or epitope-binding fragment;
- (d) screening said expressed antibody or epitope-binding fragment for said improvement, thereby preparing an improved antibody or epitope-binding fragment.

60. An improved antibody or epitope-binding fragment thereof that specifically binds to CD33, said improved antibody or antibody fragment prepared by:

- (a) providing a DNA that encodes an antibody or epitope-binding fragment thereof comprising at least one of SEQ ID NO:9 and SEQ ID NO:10,

(b) introducing at least one nucleotide mutation, deletion, insertion or addition into said DNA such that the amino acid sequence of said antibody or epitope-binding fragment encoded by said DNA is changed;

(c) expressing said antibody or epitope-binding fragment;

(d) screening said expressed antibody or epitope-binding fragment for said improvement, thereby preparing an improved antibody or epitope-binding fragment.

61. The improved antibody or antibody fragment of claim 59 or 60, wherein said improvement is an increased affinity for CD33.

62. The improved antibody or antibody fragment of claim 59 or 60, wherein said at least one nucleotide mutation, deletion, insertion or addition is made by a method selected from the group consisting of oligonucleotide-mediated site-directed mutagenesis, cassette mutagenesis, error-prone PCR, DNA shuffling and use of mutator-strains of *E. coli*.

63. An isolated polynucleotide encoding the antibody or epitope-binding fragment thereof of claim 1 or 2.

64. An isolated polynucleotide encoding a light or heavy chain of the antibody or epitope-binding fragment thereof of claim 1 or 2.

65. A recombinant vector comprising the polynucleotide of claim 63.

66. A recombinant vector comprising the polynucleotide of claim 64.

67. A host cell transformed with the recombinant vector of claim 65.

68. A host cell transformed with the recombinant vector of claim 66.

69. A method for producing an antibody or epitope-binding fragment thereof having the ability to bind CD33, said method comprising (a) culturing a host cell as claimed in claim 67 under conditions such that said host cell expresses the antibody or epitope-binding fragment, and (b) collecting the antibody or epitope-binding fragment so expressed.

70. A method for producing an antibody or epitope-binding fragment thereof having the ability to bind CD33, said method comprising (a) culturing a host cell as claimed in claim 68 under conditions such that said host cell expresses the antibody or epitope-binding fragment, and (b) collecting the antibody or epitope-binding fragment so expressed.

71. A method for obtaining CD33 from a biological material, said method comprising:

(a) contacting a biological material with the antibody or epitope-binding fragment thereof of claim 1 or 2,

(b) permitting the antibody or epitope-binding fragment of claim 1 or 2 to bind to CD33 in said biological material, and

(c) isolating the antibody or epitope-binding fragment bound to CD33 from the biological material, thereby obtaining CD33 from a biological material.